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Plant-derived flavones and flavonols: Natural antioxidants

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Abstract
In the present-day research, natural compound become the hot point of study for the safe and effective drug. Flavonoids are one of the important secondary plant metabolites. Flavone and flavonols are the major class of flavonoids, important biologically active plant-derived natural compounds. So search of new and plant-derived natural flavone and flavonols, having radical scavenging activity is of major attention to the scientists now. The present review includes 63 new examples of naturally occurring flavones and flavonols having antioxidant potential reported during the period of 2005 to Jan, 2015. These flavones and flavonols are found either as aglycones or as glycosides, comprising flavones, flavone glycosides, flavonols and flavonol glycosides. The main topics addressed are source, structure, antioxidant activity. The review cites 78 references.

Keywords: Natural flavones and flavonols, antioxidant, radical scavenging

1. Introduction
Mother Nature is an inexhaustible source of biologically active chemical entities [1]. Apart from the physiological role in plants, plant-derived natural compounds are now important for human health for their different biological activities and these natural compounds become the lead molecules for discovering different drugs for the treatment of various diseases [2-3]. Thus, nature-derived molecules are now proved themselves as important sources for pharmacologically active agents and so these are being employed in drug design [4-8]. Plants are the major source of all these important compounds. So, plant derived products attract the attentions of the scientists from different fields for their immense biological activities and natural products become the focuses for searching drugs [9-16]. Thus, biological activities of all these natural products are one of the key points of the recent research.
Among the natural compounds, flavonoids are of much interest of the chemists for their wide distribution in the plant kingdom and immense biological activities [17-19]. One of such important activities is their radical scavenging or antioxidant activities [20-21].
Flavones and Flavonols are two major sub-classes of flavonoids. Flavones, a class of benzopyrone derivatives show diverse biological activities [22-23]. Most important of them is antioxidant activity. Flavonols are the other class of flavonoids which are important natural antioxidants [24-25]. The present resume describes new naturally occurring flavones and flavonols with antioxidant activities reported during the period of 2005 to Jan, 2015. The review focuses on the sources, structures and antioxidant activities of the reported flavones and flavonols.

2. Chemical Structures: Flavones and Flavonols are major class of flavonoids which contain mainly aryl substituted benzo-□-pyrone group. This resume describes 63 new natural flavones and flavonols having antioxidant potentials reported during the mentioned period. Based on the chemical structures of the reported flavones and flavonols, all the compounds are broadly classified into flavones, flavones glycosides, flavonols, flavonol glycosides.

2.1 Flavones: Flavones are class of compounds which contain benzo-□-pyrone group having an phenyl moiety at 2 position. Here structure nos 1-11 represent this group. Here all the flavones are simple flavones having different substitutions. This group is represented by Fig.1 and Table-1.

2.2 Flavones Glycosides: when any glycoside is attached with Flavone, they are classified as Flavones glycosides. Structure no 12-26 represents this group. In this group, 12, 13, 18, 20 and

25-26 are mono glycosides of flavones and other group members are bi or poly-glycosides of flavones. Chemical structures of this group are given in Fig.2 and the names are tabulated in Table-2.

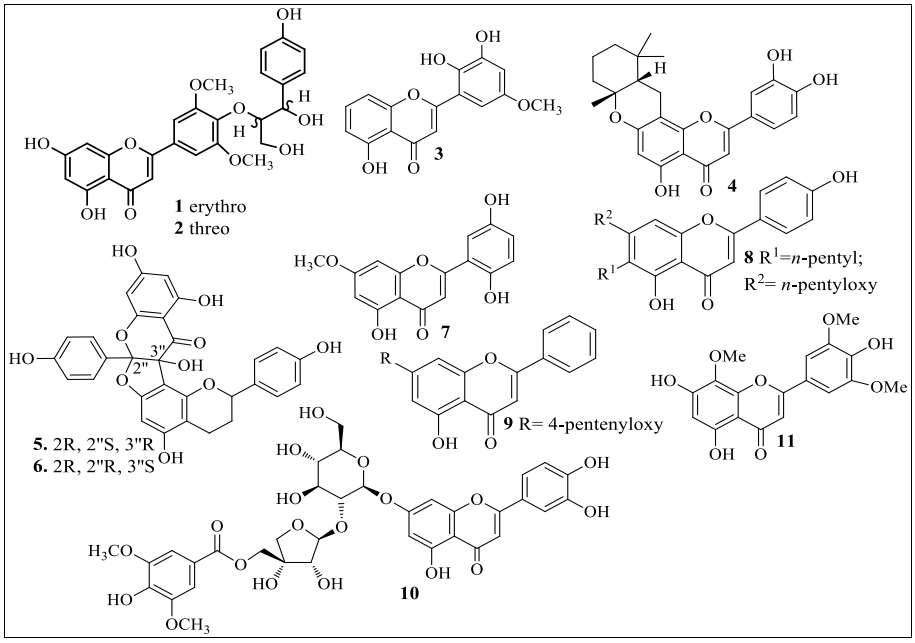

Fig 1: Chemical structures of Flavones

2.3 Flavonols: when flavone contains hydroxyl group is at 3 position, the compound is refer to as flavonols. Structure nos 27-35 represent this group. Here, structure no 34-35 are pyrano-flavonols and other members are substituted flavonols. The structures are given in Fig 3 and names are listed in Table-3.

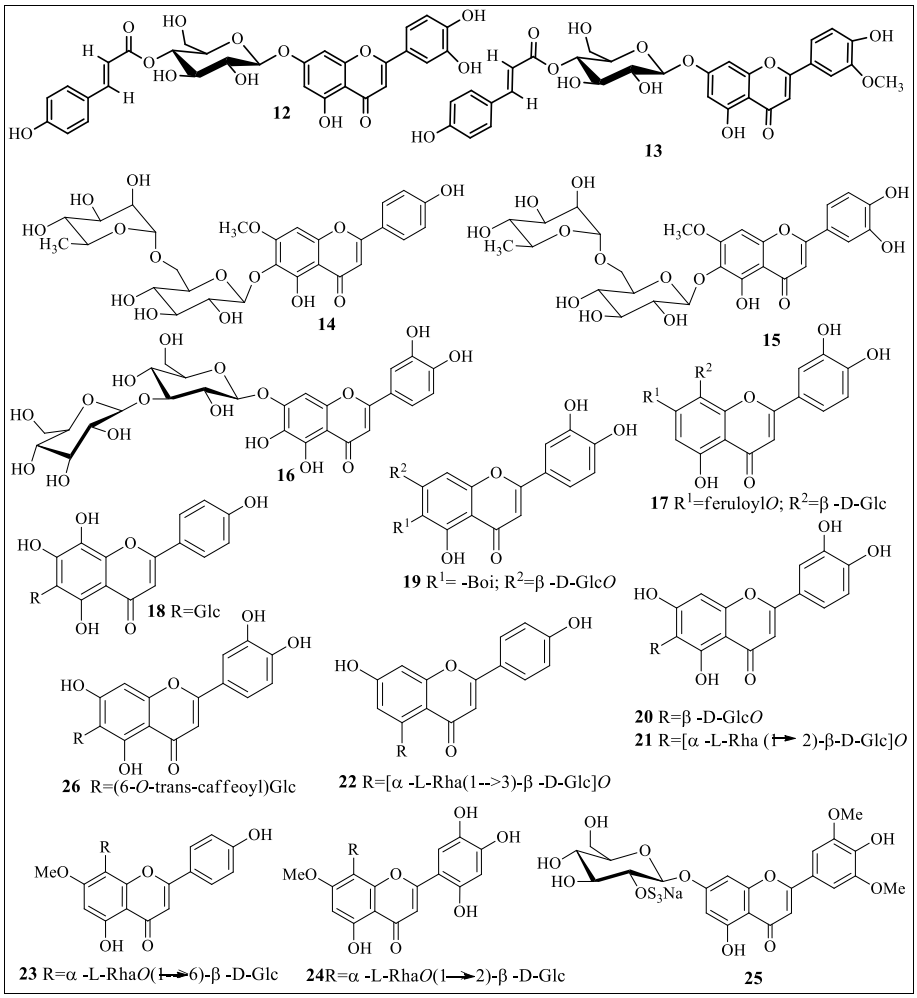

Fig 2: Chemical structures of Flavone Glycosides

2.4 Flavonol Glycosides: if the flavonol contains any glycoside at any position the compound is called flavonols glycoside. Structure nos 36 - 63 refer to this group. Structure 39, 43-44 and 56 are mono-glycoside of flavonols since these contain single glucose or any carbohydrate molecule. Other members of this group contain bi or poly carbohydrate molecules. The structures are given in Fig. 4 and compounds are listed in Tabla-4.

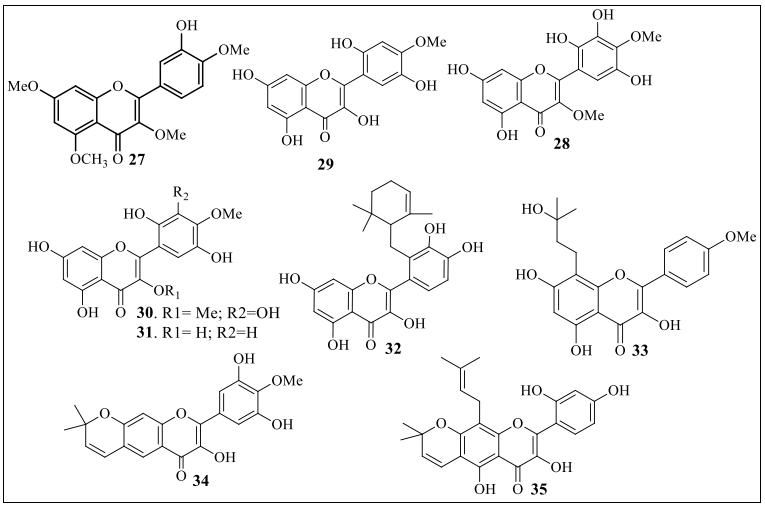

Fig 3: Chemical Structures of Flavanols

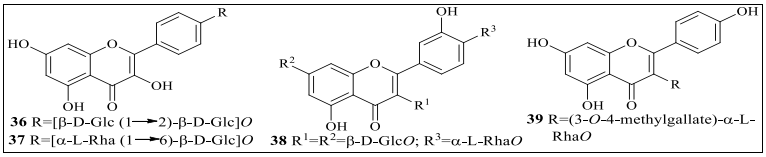

Fig 4: Chemical Structures of Flavonol Glycosides

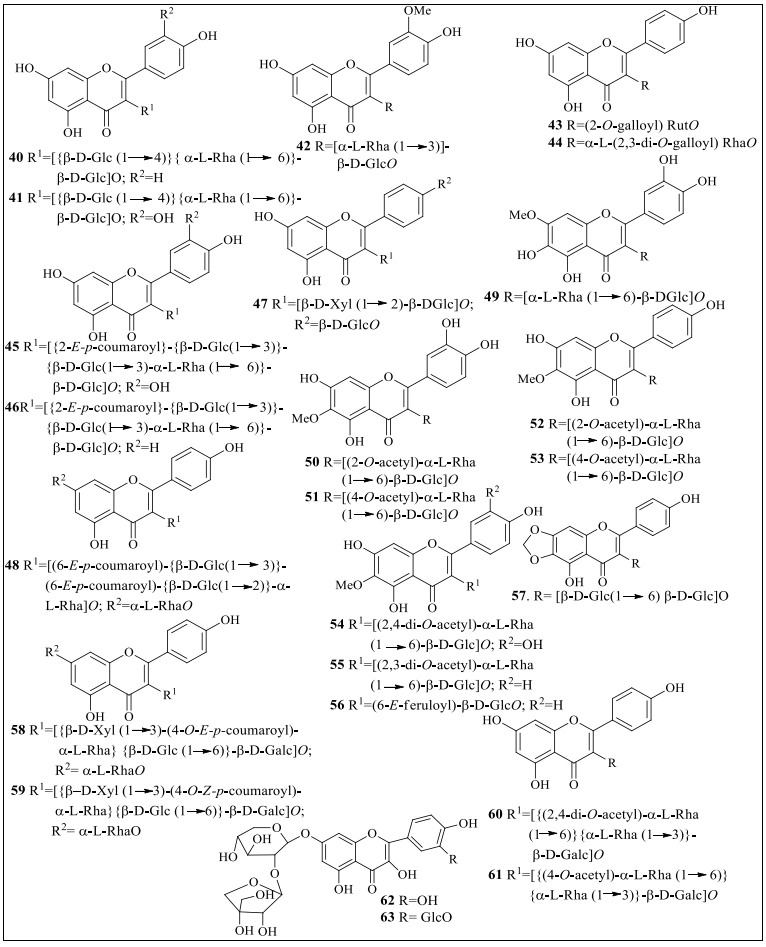

Fig 4: Chemical Structures of Flavonol Glycosides (Contd…)

3. Antioxidant Activity of the reported Flavones and Flavonols:

Any substance that delays, prevents or removes oxidative damage to a target molecule can be described antioxidants as defined by Halliwell and Gutteridge [26]. Main function of these substances is to prevent the damage to cellular components caused by chemical reactions with free radicals [27, 28]. So in living system, generation of any free radicals is a matter of considerable concern. In all living systems, free radicals so produced are reactive and can attack various biological systems. Thus, depending upon the path of the reaction of the free radicals generated, many complications in the body are developed which ultimately leads to some diseases. Nature derived polyphenolic compounds are found to show antioxidant activities mainly due to their redox properties. These natural antioxidants quench singlet and triplet oxygen, or decompose peroxides. The plants produce such polyphenolic compounds such as flavonoids as a defense against adverse conditions. Naturally occurring flavonoids have been known to possess immense biological activities including significant antioxidant efficacy. The antioxidant effect of these flavonoid molecules can be attributed due to their radical-scavenging activity and metal-chelating properties, of which the former may dominate [29, 30]. The antioxidant capabilities of many natural flavonoids are stronger than Vitamin C or E, commonly used antioxidants [31]. Flaones and Flavonols are important class of flavonoids having these antioxidant properties.

Flavones and flavonols can prevent the damage resulted by free radicals by the different mechanisms. These are i) scavenging of reactive oxygen species (ROS) [8, 28], ii) activation of antioxidant enzymes [32], iii) metal chelating activity [25, 33], iv) inhibition of oxidases [34, 35] v) reduction of α-tocopheryl radicals [35,36] etc.

Here, antioxidant activities of the reported flavones and flavonols are discussed. Antioxidant properties are evaluated with DPPH, Cytochrome C reductase NBT assay, ABTS assay etc.

3.1 Activities of Flavones

Five bioactive flavonoid constituentsalong with two new flavones (1, 2) of *Calamus quiquesetinervius* were evaluated by Chang and his co-workers for their radical scavenging ability of the hydroxyl radical (·OH) and superoxide anion ($\cdot O_2^-$) using an ultra weak CL assay. Most of the tested isolates were found to have significant scavenging activities (IC_{50} 0.34-17.18 μg/mL) against the hydroxyl radical while they were found to show moderate or weak scavenging efficiency on the superoxide anion compared with Trolox. From the structure-activity relationship, it might be argued that the tricin-type analogues 1, 2 possess antioxidant capacities against the hydroxyl radical rather than superoxide anion. Compounds 1 and 2 showed moderate radical scavenging activity due to lack of *ortho*-methyl group on the aromatic ring of the flavonoid derivatives [37]. A flavone, 5,7,2'-trihydroxy-5'-methoxyflavone (3) of *Gnetumm acrostachyum* showed weak radical scavenging activity (IC_{50} 19.90 mM) in DPPH assay [38]. The prenylated flavonoid 4, isolated from the rhizomes of *Helminthostachys zeylanica*, was found to show inhibitory activities on either superoxide anion generationor elastase release by human neutrophils informyl-*L*-methionyl-*L*-leucyl-*L*-phenylalanine/cytochalasin B (FMLP/ CB) assay [39]. The compounds 4 was reported to show inhibitory activities on FMLP/CB induced superoxide anion generation and FMLP/CB-induced elastase release by human neutrophils with IC_{50} values of 3.76 and 2.50 μM, respectively [39].

Two biflavonoids, daphnogirins A (5) and B (6), isolated from *Daphne giraldii* were found to possess significant antioxidant efficacy compared with Trolox as assessesed in oxygen radical scavenging assay using fluorescence decay induced by 2,2′-azobis(2-amidinopropane) dihydrochloride technique [40].

5,2',5'-Trihydroxy-7-methoxyflavone (7), isolated from the rhizomes of *Abacopteris penangiana*, was evaluated to show significant antioxidant activity*in vitro* and a protective effect on dopamine-induced neurotoxicity in PC12 cells [41].

Lawsochrysin (8) and Lawsochrysinin (9), two new flavones isolated from leaves of *Lawsonia alba* Lam., were evaluated for radical scavenging activity with DPPH assay using Propyl gallate as the standard. Percentages of radical scavenging activity (%RSA) were determined in the experiment. It was reported that the %RSA of the compound 8 and 9 were resulted as 2.44 and 17.73, respectively, for the two flavones while 90.31% was the value for the standard. So, two flavones were found weakly antioxidant against the DPPH radical [42].

Six flavones along with new one (10), isolated from leaves of *Teucrium polium*; were undergone testing for antioxidant activity by measuring their free radical scavenging efficacies using two different assays, the ABTS radical cation decolorization assay and the DPPH radical scavenging activity assay. Results were expressed as Trolox Euqivalent (TE). Compounds 10 exhibited a massive reduction of the target radicals and reported as potent antioxidant. The IC_{30} values of the flavone 10 in DPPH and ABTS assays were 13.85 and 55.05 μM, respectively [43]. Flavone (11) along with other isolated compounds was screened for antioxidant activity with DPPH assay. The flavone was found moderate antioxidant with IC_{50} value as 6.45 μg/mL (16 μM) [44].

3.2 Activities of Flavone Glycosides

Two flavonoids **12** and **13** isolated from whole plant of *Mallotus metcalfianus* were found to show antioxidant activity with DPPH assay as reported by Riviere group [45]. It was described that IC_{50} values of the 12 and 13 were determined as 10.0 μg/mL and 52.2 μg/mL, respectively [45]. Compounds 14 and 15 isolated from *Pterogyne nitens* showed antioxidant activities in both DPPH and ABTS assay with respective IC_{50} values of 14.7 and 15.3 μM, respectively, for compound 14 and 11.0 and 5.0 μM, respectively, for compound 15 [46]. The flavone constituent 16 of *Globularia alypum* was found to have potent antioxidant properties against DPPH radical with IC_{50} values 8.0 μM, thereby increasing their ability to efficiently scavenge free radicals [47]. Wu *et al*. [48] reported an antioxidant flavone-*C*-glucoside (17) from *Gentiana piasezkii* having potent DPPH radical scavenging properties with IC_{20} value of 5.20 μM [48]. The flavone 18 and the isolates also exhibited significant antioxidant activity against luminol-dependent chemiluminescence assay [49]. The flavone glycoside 19, isolated from the leaves of *Fargesia robusta*, was found to exhibit potent antioxidant activity in the TEAC assay. Nevertheless, it showed the highest antioxidant capacity in the ORAC assay among the tested compounds, the antioxidant efficacy of 19 was determined as 0.332 in TEAC assay and 26.8 in ORAC assay [50]. Two flavonoid *C*-glycoside

derivatives, isoorientin (20) and isoorientin 2"-*O*-α-L-rhamnoside (21), from *Sasa borealis* showed significant free radical scavenging activity against DPPH with IC_{50} values of 9.5 and 34.5 μM, respectively. Besides, these two flavones glycosides were found to be strong cytoprotective against ^{t}BuOOH-induced oxidative damage in HepG2 cells, at very low concentrations of 1.1 μM and 0.8 μM respectively [51]. Bae *et al.* described the isolation of new flavones glycoside (22) from leaves of *Cephalotaxus koreana*. It was reported that this flavones glycoside 22 was found strong antioxidant in superoxide radical scavenging assay with IC_{50} value of 13.0 μM. It was found to be weak antioxidant against 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assay as was evidenced by its high IC_{50} value as >100 μM [52].

Two new *C*-glycosyl Flavonoids celtiside A (23) and B (24), isolated from *n*-butanol-soluble fraction of *Celtisa fricana*, were also found to possess significant antioxidant efficacy by scavenging DPPH radicals with IC_{50} values of 85.5 and 75.3 □M, respectively [53]. A new flavone glycoside tricin 7-*O*-□-glucopyranoside-2"-sulphate sodium salt (25), isolated from the aqueous methanol extract of *Livistona australis* leaves, exhibited promiment antioxidant activity *in vivo* by restoring the reduced levels of GSH in the diabetic rats by 3.1% at a dose of 0.1 mg/kg [54]. Luteolin 6-*C*-6″-*O*-*trans*-caffeoylglucoside (26) isolated from *Phyllostachys nigra* was evaluated to exhibit significant antioxidant potential and the antioxidative efficacy of the flavone glycoside 26 was measured as 1.9937, 1.6601 and 0.7095 nM equivalents of Trolox at 4.0, 0.4 and 0.04□M concentrations, respectively [55].

3.3 Activities of Flavonols

The new flavone 27, isolated from the leaves of *Goniothalamus tenuifofius*, was reported to show moderate *in vitro* free radical scavenging activity against DPPH with 11.49% inhibition at a dose of 40 □g/mL. it was also suggested that antioxidant activity of the compound (27) was due to the presence of free hydroxyl group in the molecule [56]. Two flavonols 28 and 29, isolated from twigs of *Eriosemaro bustum*, were also found to show antiradical (DPPH) activity as reported by Eloff *et al* [57]. Two compounds were found strong antioxidants as IC_{50} values of the 28 and 29 were determined as 1.13 and 1.19 □g/mL respectively [57].

Robusflavone A (30) and B (31), new flavones from the plant *Eriosema robustum*, were reported to be antioxidant and this antioxidant properties were not much significant as evidenced by their IC_{50} values 1.13 and 1.19 mg/mL, respectively. But in comparison to the IC_{50} value (1.00 mg/mL) of the reference used, Ascorbic acid, these new flavones (30- 31) were said to be strong antioxidant as described by the author [58].

The prenylated and glycosylated flavonoid 32, isolated from the rhizomes of *Helminthostachys zeylanica*, was found to show inhibitory activities on either superoxide anion generationor elastase release by human neutrophils informyl-*L*-methionyl-*L*-leucyl-*L*-phenylalanine/cytochalasin B (FMLP/ CB) assay [39]. The compound 32 showed inhibitory activities on FMLP/CB induced superoxide anion generation and FMLP/CB-induced elastase release by human neutrophils with IC_{50} values of >10 and 0.98 □□M, respectively [39].

New flavonoids, wushanicaritin (33), isolated from the whole herb of *Epimedium wushanense* T.S. Ying, was tested for their radical scavenging properties using Vitamin C as reference. From the experiment, it was observed that 33 was antioxidant comparable to vitamin C as it was evidenced by IC_{50} value of 33 as 35.3 μM, comparable to that of Vitamic C (IC_{50} 32.0 μM) [59]. The scavenging effect of the a new prenylated flavonoids, lanneaflavonol (34) and other compounds, isolated from the roots of *Lannea alata*, on the stable free radical DPPH was evaluated using Ascorbic acid, a standard antioxidant, as reference. It was shown that the new compound 34 exhibited strong radical scavenging activity. The flavonoid 34 exhibited dose dependent radical-scavenging activity in the presence of the DPPH radical. The percentage radical scavenging activity for the isolated flavonol glycosides were measured at five concentrations like 6.25, 12.50, 25.0, 50.0 and 100 □g/mL and the results were reported as 23.8, 31.9, 48.8, 65.7 and 75.0%, respectively at those concentrations. The mean percentage of radical scavenging was resulted as 49.06 while that value for standard Ascorbic acid was 95.5% [60].

New flavonol (35) and other isolates were isolated from roots of *Eriosema chinense*. All the compounds were tested for their DPPH radical scavenging properties using BHT as reference. It was observed that all the isolated compounds including flavonol 35 were found antioxidant. Among the all compounds, flavonol 35 was the most active compound. This new flavonol (35) was found significantly antioxidant with IC_{50} value as 0.035 □M which was comparable with the IC_{50} value (0.039mM) of the reference, BHT [61].

3.4 Activities of Flavonol Glycosides

The scavenging potential of the flavonoid glycosides 36 and 37, isolated from the plant *Evolvulus alsinoides*, was studied and found to inhibit the formation of respective superoxide (O_2^{-}) and hydroxyl ($^{\cdot}OH$) radicals in the range of 18-33% at 100 μg/mL and 24-49% at 200 μg/mL concentrations [62]. The flavonol derivative moricandin (38) was found to have potent scavenging activity against DPPH, TEAC and other tested reducing power assays [63]. The TEAC of 38 was measured 3.4 times lower (TEAC value 1.23 □M) than that of quercetin (TEAC value 4.26 □M), which is in accordance with structure antioxidant activity relationships of flavonoid. In the reducing power assay, the formation of Fe^{2+} in the reduction of Fe^{3+}/ferricyanide complex by antioxidants is monitored at 700 nm and compound 38 was proved to be the most active, with IC_{50} values of 33.5 □g/mL. In the DPPH model system, it showed 60% inhibition of radical-scavenging activity at the lowest tested concentration of 15 □g/mL [63]. A kaempferol derivative, pterogynoside (39), isolated from fruits of *Pterogyne nitens*, was evaluated for the antioxidant activity by measuring its free radical scavenging effects using two different assays, the ABTS radical cation decolorization assay and the DPPH radical scavenging activity assay. Compound 39 showed antioxidant activity against ABTS radical with IC_{50} value of 8.10 □g/mL and against DPPH with IC_{50} value of > 80.0□□g/mL [64]. Nugroho and his groups [65] isolated two new flavonol glycosides 40 and 41 from the *Lamiumam plexicaule*. These isolates were reported to exhibit *in vitro* anti-oxidative activity in DPPH assay. The quercetin glycoside 41 exhibited stronger activity against DPPH radical than the kaempferol glycoside 40 as evidenced by EC_{50} values for the compounds 40 and 41 which were determined as 55.9, and 17.5 □g/mL, respectively [65]. A new flavonoid isorhamnetin-3-*O*- [-□-L-rhamnopyranosyl-(1→3)]-□-D-glucopyranoside (42) along with two other known flavonoids

were isolated from *Alhagi maurorum* [66]. All the isolated compounds were evaluated for their antioxidant potential using DPPH free radical scavenging assay. Compound 42 exhibited weak activity with IC_{50} value of 357.7 □g/mL [66]. The flavonol derivative, kaempferol 3-*O*-(2″-*O*-galloylrutinoside) (43) isolated from *Nymphaea candida*, was found to exhibit significant antioxidant activity estimated by *in vitro* measurement of low-density lipoprotein (LDL) susceptibility to oxidation, and determination of malondialdehyde (MDA) levels in rat brain. The percentage-increase of conjugated diene formation of LDL and inhibition rate of MDA was determined as 19.67 and 140.3%, respectively, at a dose of 0.01 g/L [67].

The scavenging effect of flavonol compound 44, isolated from the leaves of *Koelreuteria henryi*, on the stable free radical DPPH was examined by Lee *et al.* using Trolox as the standard [68]. It was shown that chemical entities with catechol or pyrogallol functionalities would exhibit strong antioxidant activities [69]. This was also observed in 44, which possessed at least one catechol group or pyrogallol group in their structures, and exhibited significant DPPH radical-scavenging activity with respective IC_{50} value of 3.6 □M when compared with the positive control, Trolox (IC_{50} 22.1 □M) [68]. Two acylated flavonoid tetraglycosides 45 and 46, isolated from *Camellia sinensis*, were reported to show radical scavenging activity against DPPH radical with EC_{50} values of 30.5 and 487.2 mM, respectively [70]. Jo *et al.* (2006) described the antioxidative activity of the flavonol derivative 47 in three different tests [71]. The compound 47 was evaluated for antioxidant activity against three assays. The compound,47, was evaluated to show potent activity with IC_{50} value 5.28 □M in the hydroxyl radical (·OH) inhibitory activity test, 82.21□□M in the total ROS (reactive oxygen species) inhibitory activity test and 13.53 □□M in the peroxynitrite ($ONOO^-$) scavenging activity test [71].

A new flavonol glycoside, wushankaempferol (48), isolated from the whole herb of *Epimedium wushanense* T.S. Ying, was tested for their radical scavenging properties using Vitamin C as reference. The compound 48 was found to have weak scavenging activity as it was revealed by very high IC_{50} value of 443.7 μM as compared to that of reference, Vitamin C (IC_{50} 32.0 μM) [59].

Flavonol glycosides (49-56) were isolated from the flowers of *Paepalanthus geniculatus* Kunth as described by do Amaral *et al.* [72]. All these flavonols were tested for antioxidant activity with TEAC assay and the results were given as TEAC values which were equivalent of Trolox solution with antioxidant activity at 01mM concentration of the tested sample. All these compounds (49-56) were reported as antioxidants and their TEAC values were compared with Quercetin, Quercetin-3-O-glycoside and Kaempferol-3-O-glucoside which were taken as standards in the experiments. The TEAC value of the compounds 49-56 were reported as 1.54, 1.37, 2.16, 1.00, 0.96, 1.21, 1.39 and 0.98 mM, respectively, as compared to the respective TEAC values of the three standards as 1.86, 1.78 and 1.17 mM [72].

Flavonol glycoside (57) along with other compounds, isolated from the aerial parts of *Chenopodium foliosum* Asch, was evaluated for antioxidant activity against DPPH free radical using Vitamin C anf BHT as the reference. Compound (57) was found weakly antioxidant against the free radical for the result was only 18% radical scavenging activity for the compound at 100 □M concentration compared to high value of 97.7% for Vitamin C and 48% for BHT at the same concentration [73].

Compounds 58 and 59, isolated from leaf of *Baphia nitida*, were found to display a mild antioxidant activity in the *in vitro* Peroxynitrite assay with EC_{50} values of 62 □M and 19 □M, respectively. These compounds were said to be weak antioxidants because these EC_{50} values were higher than those of Gallic acid (4.9 □M), taken as reference [74].

Kaempferolglycosides 60 and 61 were demonstrated to exhibit dose-dependent activity in scavenging 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radicals, superoxide anion radicals, and hydroxyl radicals, and also to inhibit lipid peroxidation of mouse liver homogenate *in vitro* [75].

These two new compounds (62-63) were evaluated for radical scavenging activity with DPPH assay using Butylated hydroxytoluene (BHT) and Ascorbic acid as reference compounds. These two flavonols 62 and 63 were reported to exhibit stronger radical scavenging activity with IC_{50} values 2.81 and 10.41 □mol/L, respectively. Both these compounds were found stronger antioxidant in DPPH assay than those of BHT and L-Ascorbic acid which were reported to have IC50 values as 75.38 and 16.47 □mol/L, respectively [76].

4. List of Flavones and Flavonols: All the new flavones and flavonols with antioxidant potentials reported during the time are given here in tabular form for easy look. The plant sources of the isolated compounds are also given. The compounds are tabulated according to the classification mentioned earlier.

Table 1: Names and source of flavones

Sl. No.	Compound (Structure No.)	Source Plant (Family)	Reference
1	Calquiquelignan D (1)	*Calamus quiquesetinervius* (Arecaceae)	[37]
2	Calquiquelignan E (2)	*Calamus quiquesetinervius* (Arecaceae)	[37]
3	5,7,2'-trihydroxy-5'-methoxyflavone (3)	*Gnetum macrostachyum* (Gnetaceae)	[38]
4	4″a,5″,6″,7″,8″,8″a-hexahydro-5,3′,4′-trihydroxy-5″,5″,8″a-trimethyl -4*H*-chromeno [2″,3″:7,8] flavone (4)	*Helminthostachys zeylanica* (Ophioglossaceae)	[39]
5	Daphnogirins A (5)	*Daphne giraldii* (Thymelaeaceae)	[40]
6	Daphnogirins B (6)	*Daphne giraldii* (Thymelaeaceae)	[40]
7	5,2',5'-trihydroxy-7-methoxy-flavone (7)	*Abacopteris penangiana* (Thelypteridaceae)	[41]
8	Lawsochrysin (8)	*Lawsonia alba* (Lythraceae)	[42]
9	Lawsochrysinin (9)	*Lawsonia alba* (Lythraceae)	[42]
10	7-*O*-β-D-(5-O-syringyl)apiofurano syl-(1 →2)-β-D-glucopyranoside (10)	*Teucriumpolium* (Labiatae)	[43]
11	5,7,4′-trihydroxy-3,8,3′,5′-tetra methoxyflavone (11)	*Microglossa pyrifolia* Kuntze (Asteraceae)	[44]

Table 2: Names and source of flavone glycosides

Sl. No	Compound (Structure No.)	Source Plant (Family)	Reference
1	Luteolin 7-*O*-(4"-*O*-(*E*)-coumaroyl) -□-glucopyranoside (12)	*Mallotus metcalfianus* (Euphorbiaceae)	[45]
2	Chrysoeriol-7-*O*-(4"-*O*-(*E*)-coumaroyl)-□-glucopyranoside (13)	*Mallotus metcalfianus* (Euphorbiaceae)	[45]
3	Nitensoside A (14)	*Pterogyne nitens* (Fabaceae)	[46]
4	Nitensoside B (15)	*Pterogyne nitens* (Fabaceae)	[46]
5	6-hydroxyluteolin 7-*O*-laminaribioside (16)	*Globularia alypum* (Globulariaceae)	[47]
6	7-*O*-feruloylorientin (17)	*Gentiana piasezkii* (Gentianaceae)	[48]
7	Isoscutellarein 6-*C*-□-D-gluco-pyranoside (18)	*Iris pseudopumila* (Iridaceae)	[49]
8	Farobin A (19)	*Fargesia robusta* (Poaceae)	[50]
9	Isoorientin (20)	*Sasa borealis* (Poaceae)	[51]
10	Isoorientin 2-*O*-□-*L*-rhamnoside (21)	*Sasa borealis* (Poaceae)	[51]
11	Apigenin 5-*O*-□-*L*-rhamnopyranosyl -(1→3)-□-D-glucopyranoside (22)	*Cephalotaxuskoreana* (Taxaceae)	[52]
12	Celtiside A (23)	*Celtis africana* (Ulmaceae)	[53]
13	CeltisideB (24)	*Celtis africana* (Ulmaceae)	[53]
14	Tricin 7-*O*-□-glucopyranoside-2"-sulphate sodium salt (25)	*Livistona australis* (Arecaceae)	[54]
15	Luteolin 6-*C*-(6″-*O*-trans-caffeoyl-glucoside) (26)	*Phyllosta chysnigra* (Gramineae)	[55]

Table 3: Names and source of flavonols

Sl. No	Compound (Structure No.)	Source Plant (Family)	Reference
1	3'-hydroxy-3,5,7,4′-tetramethoxy flavone (27)	*Goniothalamus tenuifolius* (Annonaceae)	[56]
2	Robusflavone A(28)	*Eriosema robustum* (Fabaceae)	[57]
3	Robusflavone B (29)	*Eriosema robustum* (Fabaceae)	[57]
4	2',3',5',5,7-pentahydroxy-3,4'-dime thoxyflavone (30)	*Eriosema robustum* (Fabaceae)	[58]
5	2',3,5',5,7-pentahydroxy-4'-metho xyflavone (31)	*Eriosema robustum* (Fabaceae)	[58]
6	2-(3,4-dihydroxy-2- [(2,6,6-trimethyl cyclohex-2-enyl) methyl] phenyl)-3,5,7-trihydroxy-4*H*-chromen-4-one (32)	*Helminthostachys zeylanica* (Ophioglossaceae)	[39]
7	Wushanicaritin (33)	*Epimedium wushanense* (Berberidaceae)	[59]
8	3,5,3′,5′-tetrahydroxy-4′-methoxy-6,7-(2″,2″-dimethylchromene)-flavonol (34)	*Lannea alata* (Anacardiaceae)	[60]
9	3,5,2′,4′-tetrahydroxy-6″,6″-dimethylpyrano (2″,3″:7,6)-8-(3‴,3‴-dimethylallyl) flavone (35)	*Eriosema chinense* (Leguminosae)	[61]

Table 4: Names and source of flavonol glycosides

Sl. No	Compound (Structure No.)	Source Plant (Family)	Reference
1	Kaempferol 4′-*O*-β-D-gluco-pyranosyl-(1→2)-β-D-gluco-pyranoside (36)	*Evolvulus alsinoides* (Convolvulaceae)	[62]
2	Kaempferol 4′-*O*-α-L-rhamno-pyranosyl-(1→6)-β-D-gluco-pyranoside (37)	*Evolvulus alsinoides* (Convolvulaceae)	[62]
3	Moricandin (38)	*Moricandia arvensis* (Cruciferae)	[63]
4	Pterogynoside (39)	*Pterogyne nitens* (Fabaceae)	[54]
5	Kaempferol 3-*O*-{□-D-gluco-pyranosyl-(1→4)} {□-L-rhamno-pyranosyl-(1→6)}-□-D-gluco-pyranoside (40)	*Lamiun amplexicaule* (Lamiaceae)	[65]
6	Quercetin 3-*O*-{□-D-glucopyrano-syl-(1→4)}{□-L-rhamnopyrano-syl-(1→6)}-□-D-glucopyranoside 7(41)	*Lamiun amplexicaule* (Lamiaceae)	[65]
7	Isorhamnetin-3-*O*- [□-L-rhamno-pyranosyl-(1→3)]-β-D-gluco-pyranoside (42)	*Alhagi maurorum* (Leguminosae)	[66]
8	Kaempferol 3-*O*-(2″-*O* galloyl)-rutinoside (43)	*Nymphaea candida* (Nymphaeaceae)	[67]
9	Kaempferol 3-*O*-(2",3"-di-*O*-galloyl)-□-L-rhamno pyranoside (44)	*Koelreuteria henryi* (Sapindaceae)	[68]
10	Quercetin 3-*O*-{2^{G}-(*E*)-coumaroyl-3^{G}-*O*-□-D-glucosyl-3^{R}-*O*-□-D-glucosyl rutinoside} (45)	*Camellia sinensis* (Theaceae)	[70]
11	Kaempferol 3-*O*-{2^{G}-(*E*)-Coumaroyl-3^{G}-*O*-□-D-glucosyl -3^{R}-*O*-□-D-glucosyl rutinoside} (46)	*Camellia sinensis* (Theaceae)	[70]
12	3-*O*-□-D-Xylopyranosyl (1→2)-□-D-glucopyrano-sylkaempferol 4□-*O*-□-D-glucopyranoside (47)	*Ternstroemia japonica* (Theaceae)	[71]
13	Wushankaempferol (48)	*Epimedium wushanense* (Berberidaceae)	[59]
14	6-Hydroxy-7-methoxy quercetin-3-*O*-α-L-rhamno-pyranosyl-(1→6)-β-D-gluco pyranoside (49)	*Paepalanthus geniculatus* (Eriocaulaceae)	[72]
15	6-Methoxyquercetin-3-*O*-(2-*O*-acetyl)-α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside (50)	*Paepalanthus geniculatus* (Eriocaulaceae)	[72]
16	6-Methoxyquercetin-3-*O*-(4-*O*-acetyl)-α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside (51)	*Paepalanthus geniculatus* (Eriocaulaceae)	[72]
17	6-Methoxykaempferol-3-*O*-(2-*O*-acetyl)-α-L-rhamnopyrano syl-(1→6)-β-D-glucopyranoside (52)	*Paepalanthus geniculatus* (Eriocaulaceae)	[72]
18	6-Methoxykaempferol-3-*O*-(4-*O*-acetyl)-α-L-rhamnopyrano syl-(1→6)-β-D-glucopyranoside (53)	*Paepalanthus geniculatus* (Eriocaulaceae)	[72]

19	6-Methoxyquercetin-3-*O*-(2,4-di-*O*-acetyl)-α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside (54)	*Paepalanthus geniculatus* (Eriocaulaceae)	[72]
20	6-Methoxykaempferol-3-*O*-(2,3-di-*O*-acetyl)-α-L-rhamnopyrano-syl-(1→6)-β-D-glucopyranoside (55)	*Paepalanthus geniculatus* (Eriocaulaceae)	[72]
21	6-Methoxykaempferol-3-*O*-(6-*E*-feruloyl)-β-D-glucopyranoside (56)	*Paepalanthus geniculate* (Eriocaulaceae)	[72]
22	Gomphrenol-3-*O*-□-D-gentiobioside (57)	*Chenopodium foliosum* (Amaranthaceae)	[73]
23	Kaempferol 3-*O*-□-D-xylopyra nosyl-(1→3)-(4-*O*-*E*-*p*-coumaroyl-□-L-rhamnopyranosyl-(1→2)) [□-D-glucopyranosyl-(1→6)]-□-D-galactopyranoside-7-*O*-□-L-rhamnopyranoside (58)	*Baphia nitida*(Fabaceae)	[74]
24	Kaempferol 3-*O*-□-D-xylopyrano-syl(1→3)-(4-*O*-*Z*-*p*-coumaroyl-□-L-rhamnopyranosyl-(1→2)) [□-D-glucopyranosyl(1→6)]-□-D-galactopyranoside-7-*O*-□-L-rhamnopyranoside (59)	*Baphia nitida* (Fabaceae)	[74]
25	Kaempferol 3-*O*-α-L-rhamno-pyranosyl (1→3) (2,4-di-*O*-acetyl-α-L-rhamnopyranosyl) (1→6) β-D-galactopyranoside (60)	*Actinidia valvata (*Actinidiaceae*)*	[75]
26	Kaempferol 3-*O*-α-L-rhamno-pyranosyl (1→3) (4-*O*-acetyl-α-L-rhamnopyranosyl) (1→6)-β-D-galactopyranoside (61)	*Actinidia valvata (*Actinidiaceae*)*	[75]
27	Quercetin 7-O-□-D-apiofuranosyl-(1 → 2)-□-Dxylopyranoside (62)	*Hyssopus officinalis*	[76]
28	Quercetin 7-O-□-D-apiofuranosyl-(1 → 2)-□-D-xylopyranoside 3'-O-□-D-glucopyranoside (63)	*Hyssopus officinalis*	[76]

5. Structure-Activity relationship (SAR): The biological activity of any natural products depends upon structure of the molecule. Flavonoids having diversified substitution pattern in the structural skeleton are thus biologically active molecules. So, the antioxidant activity of the flavones and flavonols also depends upon the structural pattern of these molecule. These molecule, being polyphenolic, shows different activity according to the extent of conjugation present in the molecule and position and freeness of the hydroxyl groups.

Flavonoids, natural polyphenols, were reported to have antioxidant activity. This antioxidant activity of flavonoids are more potent when hydroxylation at position C-3 of C-ring, a double bond at C-2, C-3 along with a carbonyl group at C-4, in addition to the ortho- and the paradihydroxylations as well as the ortho-methylation of B-ring [6].

The number of hydroxy groups and particularly the presence of a B-ring catechol group might be responsible for this antioxidant capacity [35]. Comparisons of the hydroxyl radical scavenging activities of the compounds showed that the C_2-C_3 bond in C-ring of tricin-type of flavove derivatives enhances antioxidant activity. Thus, Compounds 1 and 2 showed moderate radical scavenging activity due to lack of *ortho*-methyl group on the aromatic ring of the flavonoid derivatives [37]. Polyhydroxylation of the aromatic rings is one of the structural requirements for antioxidant and free radical scavenging function of flavonoids; hence, flavonoids possessing a higher number of hydroxy groups usually exhibit stronger anti-oxidative effect [77].

Likhitwitayawuid *et al.* suggested that the activity of the compound is attributed due to the presence of free hydroxyl group at C-3′ [56]. Comparing the results for compound 35 and the reference, it was revealed that the presence of free OH at C-3, C-2′ and C-4′ are essential for stronger radical scavenging activity whereas the presence of free OH at C-5 has minor effect for the activity [61]. The investigators of compound 39 suggested that glycosylation at C-7 and C-4′ reduces the radical-scavenging capacity but the attachment of glucose to the OH-3 position does not seem to have any negative effect on the antioxidative capacity [63]. The activity of quercetin glycoside (41) with one more hydroxy group in their B-ring was more potent than that of kaempferol with one less hydroxyl group [65]. Compound 62 was more active than compound 63 because of the substitution pattern of the ring B. Monohydroxyl group in ring B and hydroxyl at C-3' and C-4' are very important for the absorption of oxygen radical [76, 78].

6. Conclusion

The defense mechanism of natural flavonoids in biological system is attributed to their antioxidant activities. Since the damage caused by free radicals has been associated with several degenerative diseases, natural molecules with scavenging activity of these free radicals are of much interest to the biological scientists. Considering the impact of damage by free radicals on living body, research on new compounds with antioxidant activity becomes essential. Natural flavones and flavonols being polyphenolic compounds has the properties to arrest the free radicals and thus they are very good antioxidant. Again, natural flavones and flavonols are metabolized as such and removed from the body. These flavones and flavonols are, thus, important for the medicinal chemists to search for natural antioxidants. Search of new natural flavones and flavonols with antioxidant properties becomes attractive for scientists. Thus, it is felt pertinent to sum up new natural flavones and flavonols which can help all scientists to search for new natural antioxidants. This resume will surely enlightens the research on antioxidant flavonoids.

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Abbreviations: Glc = glucopyranosyl; Rha = rhamnopyranosyl; Gal = galloyl; Sp =sophorosyl; Xyl = xylopyranosyl; Galc = galactopyranosyl; Rut = rutinosyl; Lam = laminaribiosyl; Boi = boivinopyranoside;
Galloyl = 3,4,5-trihydroxybenzoyl; Sophorosyl = □-D-Glc(1→3)-□-D-Glc;

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